Selective oxidation of substituted xylenes to toluic acids by hypochlorite–Ru system under phase transfer conditions

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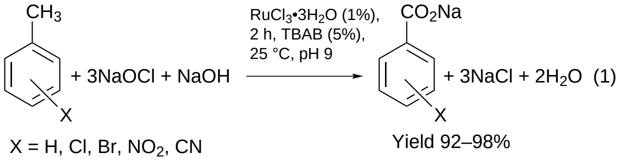
Instantaneous aqueous extraction of toluic acid salts is the basis for a novel selective process for the oxidation of a single methyl group of various xylenes; aqueous hypochlorite is inert towards methylbenzenes at pH higher than 9.0, however, in the presence of an organic solvent, a Ru catalyst and a phase transfer agent, rapid oxidation to benzoic acids is observed at 25 °C.

The combination of ruthenium tetroxide as catalyst with sodium hypochlorite as primary oxidant was shown to be effective in the oxidation of olefins, alkynes and aromatic rings. The system could be improved by the addition of a phase transfer catalyst (PTC).[1] We have shown that methylbenzenes can readily be transformed into benzoic acids at room temperature upon exposure to aqueous sodium hypochlorite at pH 9–10 in the presence of $RuCl_3$ and tetra-*n*-butylammonium bromide (TBAB) catalysts in a two phase system [eqn. (1)].[2]



In a recent study we subsequently observed that this system is also capable of converting alkanes and cycloalkanes into ketones accompanied by some chlorinated products,[3] similar to other ruthenium catalyzed oxidations.[4]

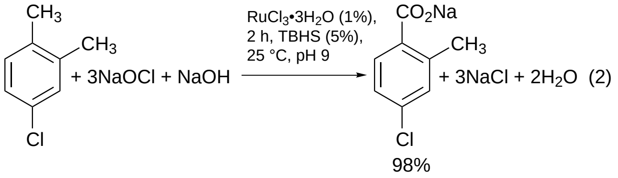
A major feature of the Ru–NaOCl–PTC system in the oxidation of methylbenzenes is the instantaneous transport of the benzoic acid product as it forms into the basic aqueous phase thus allowing the facile separation of the product from the catalysts which abide in the organic phase ready for reuse in a succeeding reaction batch. This unique characteristic can also be the foundation for the design of a continuous catalytic liquid–liquid oxidation process.

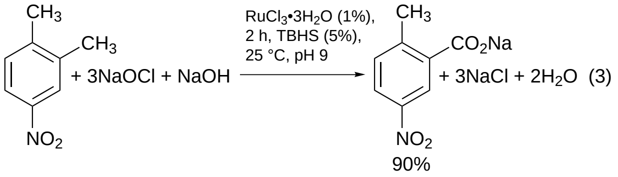
The instantaneous extraction of benzoic acids (as sodium salts) into the aqueous phase can also be utilized for a selective oxidation of one methyl group in polymethylbenzenes such as xylenes or trimethylbenzenes. This is the subject of this communication. We have found that when xylenes are reacted under the above conditions complete conversion is achieved after two hours with only one methyl group selectively oxidized to the corresponding carboxylic acid.

Toluic acids are obtained in the autoxidation of xylenes in the presence of a cobalt(II) catalyst in acetic acid solvent but high selectivity to the desired products is obtained only at relatively low conversions.[5,6] At higher conversions the major product is the dicarboxylic acid. Thus alternative methods were proposed for the preparation of substituted toluic acids. Typical examples are the hydrolysis of toluonitriles[7,8] (obtained by diazotization of anilines in presence of CuCN) and the oxidation of methylacetophenones *via* the haloform reaction.[9,10]

Our new oxidation system is demonstrated with the following typical procedure. 4-Chloro-*o*-xylene (4.6 g, 33 mmol), tetra-*n*-butylammonium hydrogen sulfate[11] (TBHS, 0.47 g, 1.6 mmol) and ruthenium chloride trihydrate (70 mg, 0.33 mmol) were dissolved in 1,2-dichloroethane (25 ml) in a 300 ml flask equipped with a mechanical stirrer, a thermometer, a pH meter and a dual dropping funnel, one filled with commercial aqueous hypochlorite and the other with 20% aqueous NaOH. Aqueous hypochlorite (200 ml) was added into the flask with stirring at a rate of 1.5 ml min^{-1} while keeping the system at 25 °C. The pH was maintained throughout the process at 9.0 by manual gradual addition of 20% aqueous NaOH (28 ml in total was added). After two hours the aqueous phase was separated, acidified with 20% aqueous sulfuric acid to pH 3 and the precipitate was filtered and dried to give 4-chloro-2-methylbenzoic acid (5.50 g, 98%), mp 170 °C, were obtained. The structure of the product was confirmed by comparison with an authentic sample.

Interestingly, when 4-nitro-*o*-xylene was reacted under an identical procedure, the *meta* methyl group was oxidised to yield 2-methyl-5-nitrobenzoic acid (mp 176 °C) in 90% yield. This is shown in eqns. (2) and (3).

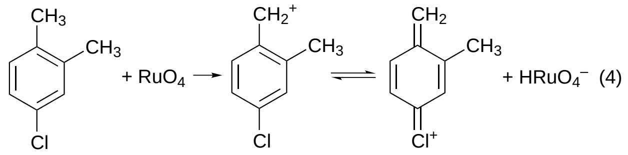




The reaction was found to be of a general nature with numerous substituted xylenes. These experiments have revealed the following observations. (a) When unsubstituted xylenes or xylenes bearing electron donating groups (such as methoxyxylenes) are reacted under the above conditions, the major reaction taking place is ring chlorination accompanied with some side chain chlorination. The ring chlorinated xylenes were further oxidized to the corresponding toluic acids resulting in a mixture of toluic acids and side-chain chlorinated xylenes. (b) In oxidizing xylenes bearing an electron withdrawing substituent which also has a lone pair of electrons available to stabilize the carbonium ion, such as bromine or chlorine, the methyl group *para* or *ortho* to the substituent is oxidized. (c) In reactions of xylenes with electron withdrawing substituents not containing an unshared pair of electrons such as nitro, sulfonate or carboxylate, the methyl group *meta* to the substituent is selectively oxidized. (d) The oxidation rate is slower when substituents with stronger $-I$ effect are present. (e) No oxidation reaction is taking place in the aqueous phase thus once the toluic acid product is extracted into the water no further oxidation is observed. (f) Non-selective oxidation was realized when 4-nitro-*m*-xylene was reacted with formation of both possible toluic acids.

These observations support our originally proposed mechanism for the Ru–NaOCl–PTC system.[2] The key step is a hydride abstraction from the substrate by RuO_4 to form a carbonium ion which is promptly hydrolyzed.

With chlorine in the 4-position the carbonium ion is more stable on the *para* methyl group due to existence of canonical structures with the positive charge on the chlorine atom. Such forms are not possible when the ion is on the *meta* methyl group [eqn. (4)]. With 4-nitro substituted xylene the −I effect of the substituent destabilizing the carbonium ion, is more pronounced for the *para* methyl group resulting in activation of the *meta* methyl group.



(4)

Upon attempts to recycle the catalytic system for consecutive runs we have found some deactivation of the catalytic activity. This could be corrected by modifying the solvent with addition of a nitrile. When using a solvent mixture of 1 : 1 (w/w) 1,2-dichloroethane and benzonitrile (which is known to stabilize RuO_4 in the organic phase[12]) the catalysts could be recycled in the same solvent for seven consecutive runs without any apparent loss in activity.

Footnote and References

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